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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,526	09/12/2001	John C. Reed	P-LJ 4868	8589
23601	7590	10/06/2003	EXAMINER	
CAMPBELL & FLORES LLP 4370 LA JOLLA VILLAGE DRIVE 7TH FLOOR SAN DIEGO, CA 92122			COLLINS, CYNTHIA E	
			ART UNIT	PAPER NUMBER
			1638	

DATE MAILED: 10/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/955,526	Applicant(s) REED, JOHN C.	
	Examiner Cynthia Collins	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-46 is/are pending in the application.
- 4a) Of the above claim(s) 22-28 and 44-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 29-42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claims 29-43, filed July 2, 2003, is acknowledged. The traversal is on the ground(s) that a search of Groups I-III would not be unduly burdensome as the subject matter of Group II (a non-naturally occurring plant that ectopically expresses a nucleic acid molecule) overlaps the subject matter of Groups I (an isolated nucleic acid molecule) and III (an isolated polypeptide). This is not found persuasive because the searches of Groups I-III are not coextensive. A search of Group I requires a search for all isolated Bax-inhibitor nucleotide sequences, including an excluded Bax-inhibitor sequences (GenBank Accession AI771102) and SEQ ID NO:3), as not all of the claims are limited to a specific nucleotide sequence, whereas a search of Group II requires a search only for plants that overexpress Bax-inhibitor nucleotide sequences. A search of Group III requires a search for all isolated Bax-inhibitor polypeptides, as not all of the claims are limited to a specific amino acid sequence, whereas a search of Group II requires a search only for plants that overexpress Bax-inhibitor polypeptides. Accordingly, claims 22-28 and 44-46 are withdrawn from consideration as being directed to nonelected inventions.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, filed December 18, 2001, is attached to the instant Office action.

Specification

The Abstract is objected to because it is not commensurate in scope with the elected invention. Appropriate correction is required.

The specification is objected to because the serial number of the provisional application to which priority is claimed (60/331,371) is missing. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-30 and 32-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a non-naturally occurring plant comprising an ectopically expressed nucleic acid molecule encoding a tomato Bax inhibitor-1 (BI-1) polypeptide or any fragment thereof that retains an unspecified activity, including a tomato BI-1 having substantially the amino acid sequence of SEQ ID NO:4 or the amino acid sequence of SEQ ID NO:4, said plant being characterized by increased resistance to any unspecified biotic or abiotic stress. The claims are also drawn to a method of increasing the resistance of a plant to biotic or

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abiotic stress by ectopically expressing in a plant by any means a nucleic acid molecule encoding a tomato BI-1 polypeptide or an active fragment thereof.

In contrast, the specification describes the isolation of a nucleic acid molecule encoding a polypeptide of SEQ ID NO:4 that when expressed rescues the lethal phenotype of yeast that express a cell death promoting mammalian BAX polypeptide (page 48 line 10 through page 50 line 23). The specification indicates at page 5 line 27 through page 7 line 2 that ectopic expression of a tomato BI-1 polypeptide such as SEQ ID NO:4 in a plant would increase the resistance of the plant to abiotic or biotic stress, but the specification does not describe or characterize any plant that ectopically expresses of a tomato BI-1 polypeptide and that exhibits increased resistance to any particular abiotic or biotic stress. Furthermore, the specification does not describe or characterize any particular fragment of SEQ ID NO:4 that exhibits a specific activity, or any tomato BI-1 polypeptide that has substantially the amino acid sequence of SEQ ID NO:4.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." *Id.* Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the

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species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." Id.

Given the claim breadth and lack of defining features as discussed above, the specification fails to provide an adequate written description of the genus as broadly claimed. Given the lack of written description of the claimed products, any method of using them would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicants to have been in possession of the claimed invention at the time of filing. See Written Description Requirement guidelines published in Federal Register/ Vol. 66, No.4/ Friday January 5, 2001/Notices: pp. 1099-1111).

Claims 29-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a non-naturally occurring plant comprising an ectopically expressed nucleic acid molecule encoding a tomato Bax inhibitor-1 (BI-1) polypeptide or any fragment thereof that retains an unspecified activity, including a tomato BI-1 having substantially the amino acid sequence of SEQ ID NO:4 or the amino acid sequence of SEQ ID NO:4, said plant being characterized by increased resistance to any unspecified biotic or abiotic stress. The claims are also drawn to a method of increasing the resistance of a plant to biotic or abiotic stress by ectopically expressing in a plant by any means a nucleic acid molecule encoding a tomato BI-1 polypeptide or an active fragment thereof.

In contrast, the specification discloses the isolation of a nucleic acid molecule encoding a polypeptide of SEQ ID NO:4 that when expressed rescues the lethal phenotype of yeast that express a cell death promoting mammalian BAX polypeptide (page 48 line 10 through page 50 line 23), but the specification does not provide specific guidance for making a fragment of SEQ ID NO:4 that exhibits a specific activity, or for making a tomato BI-1 polypeptide that has substantially the amino acid sequence of SEQ ID NO:4. At page 51 line 16 through page 52 line 23 the specification also discloses that transgenic *Arabidopsis* or tobacco plants that ectopically express SEQ ID NO:4 may be assayed for resistance to specific pathogens such as *S. sclerotiorum*, turnip crinkle virus or *Pernonospora parasitica*, or specific abiotic stresses such as UV-light and heat, but the specification does not disclose how transgenic plants may be assayed for other types of biotic or abiotic stresses such as grazing, insect infestation, wind, drought, hypoxia, high salt, heavy metals, nutrient depletion, etc. Additionally, the specification also indicates at page 5 line 27 through page 7 line 2 that ectopic expression of a tomato BI-1 polypeptide such as SEQ ID NO:4 in a plant would increase the resistance of the plant to abiotic or biotic stress, but the specification does not disclose how any transgenic plant ectopically expressing SEQ ID NO:4 actually responds to any specific type of biotic or abiotic stress.

Guidance for making and using the claimed invention is necessary for enablement because the ability an ectopically expressed anti-death polypeptide such as a tomato BI-1 polypeptide to increase the resistance of a plant to biotic or abiotic stress is unpredictable. For example, Mittler et al. teach that the expression of a mammalian anti-death polypeptide in transgenic plants does not confer resistance to programmed cell death induced by viral and bacterial biotic stresses (Plant Cell, 1996, Vol. 8, pages 1991-2001, Applicant's IDS). Mittler et

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al. constructed transgenic tobacco plants expressing the human anti-death polypeptide Bcl-xL (page 1999 column 1). Expression of Bcl-xL in transgenic tobacco did not inhibit programmed cell death induced by tobacco mosaic virus or *Pseudomonas syringae* (page 1996 and Figure 7 page 1997). In light of this unpredictability, it would require undue experimentation to determine whether and to what extent the stress resistance of a plant that ectopically expresses a Bax inhibitor-1 polypeptide is increased, as the effect of a variety of different types and levels of specific biotic and abiotic stresses on the plants would have to be tested.

Guidance for making and using the claimed invention is also necessary for enablement because the ability of a nucleic acid molecule to increase the resistance of a plant to more than one type of biotic or abiotic stress simultaneously is also unpredictable. Whether a protein involved in stress resistance can affect more than one type of stress simultaneously depends on whether or not that protein functions in a pathway common to multiple stresses. For example, Liu et al. teach that two transcription factors, DREB1 and DREB2, function in two separate signal transduction pathways under low temperature and dehydration conditions respectively (The Plant Cell, 1998, Vol. 10, pages 1391-1406). The expression of DREB1 transcription factors is induced by low-temperature stress, whereas the expression of DREB2 transcription factors is induced by dehydration and high-salt stress (page 1398 Figure 6). Furthermore, overexpression of DREB1 in transgenic plants induced the expression of rd29A, a gene whose expression is induced by dehydration, high salt and low temperature stress in nontransgenic wild type plants, whereas overexpression of DREB2 did not induce rd29A expression (page 1402 Figure 11). Liu et al.'s observations indicate that plants respond to stress through independent as well as overlapping biochemical pathways. In light of this unpredictability, it would require

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undue experimentation to determine which particular stresses a plant that ectopically expresses a Bax inhibitor-1 polypeptide would have increased resistance to, as the effect of a variety of different types and levels of specific biotic and abiotic stresses on the plants would have to be tested.

Guidance for making and using the claimed invention is additionally necessary for enablement because it is also unpredictable whether a fragment of SEQ ID NO:4 or a polypeptide having substantially the amino acid sequence of SEQ ID NO:4 would retain the biological activity of SEQ ID NO:4, because a change in as few as one amino acid in a polypeptide can alter or eliminate its function. For example, Rhoads et al. (J. Biol. Chem., November 1998, Vol. 273, No. 46, pages 30750-30756) teach that mutation of Cys-128 to Ala in an *Arabidopsis* alternative oxidase caused a pronounced overall increase in enzyme activity relative to the wild-type in the presence or absence of pyruvate (page 30753 Figure 3). Mutation of Cys-78 to Ala in the same *Arabidopsis* alternative oxidase resulted in a minimally active enzyme that showed no response to added pyruvate (page 30753 Figure 3). In light of this unpredictability, it would require undue experimentation to determine which particular amino acids of SEQ ID NO:4 would need to be retained by an active fragment of SEQ ID NO:4 or a polypeptide having substantially the amino acid sequence of SEQ ID NO:4, as the effect of a variety of different changes in the amino acid sequence of SEQ ID NO:4 would have to be tested.

Given the claim breadth, the unpredictability of increasing the resistance of a plant to any or all biotic or abiotic stresses by ectopically expressing in a plant a tomato BI-1 polypeptide, and the unpredictability of an altered tomato BI-1 polypeptide retaining its biological function,

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and given the lack of guidance as discussed above, it would require undue experimentation for one skilled in the art to make and use a plant having increased resistance to a specific biotic or abiotic stress by ectopically expressing in a plant a nucleic acid molecule encoding a tomato Bax inhibitor-1 (BI-1) polypeptide or an active fragment thereof.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29-36 and 42-43, and claims dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29-32 are indefinite in the recitation of “non-naturally occurring plant”. It is unclear how a plant could be “non-naturally occurring”, because a plant is a living organism, and as such is considered to be “natural”.

Claims 29 and 42-43 are indefinite in the recitation of “an active fragment thereof”. It is unclear what activity the fragment would exhibit, as proteins can exhibit more than one type of activity, and the claim does not specify the activity retained by the fragment.

Claims 33-35 are indefinite in the recitation of “exogenous regulatory element”. It is unclear how a regulatory element could be “exogenous”, because the coding sequence with which a transgenic plant is transformed is inside the plant, as would be any regulatory element to which it is operably linked.

Claims 33-35 are indefinite in the recitation of “regulatory element”. It is unclear what the element would regulate, as the claim indicates only that it is operatively linked to a coding

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sequence, which could be affected by different types of regulatory elements in different ways. For example, a promoter could regulate transcription of a coding sequence, and a terminator could regulate the polyadenylation of a coding sequence transcript.

Claims 36 is indefinite in the recitation of “common fruit and ornamental flower plant”. It is unclear what type of plant(s) are intended by this phrase. First, does the phrase apply to plants that are simultaneously fruit and ornamental in nature, or to fruit plants and to ornamental plants? Second, it is unclear in what way such plants are “common”. For example, plants could be common because they are commonly cultivated, or they could be common because they commonly grow in a particular geographic area.

Claims 42-43 are indefinite in the recitation of “increasing”, as “increasing” is a relative term that lacks a comparative basis.

Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claim 42 is directed to a method of increasing the resistance of a plant to biotic or abiotic stress by ectopically expressing in a plant a nucleic acid molecule encoding a tomato BI-1 polypeptide, but the claim recites no method steps by which such ectopic expression could be accomplished.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 29-30 and 32-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Flinn et al. (US Patent No. 6,451,604, filed June 4, 1999 and issued September 17, 2002).

The claims are drawn to a non-naturally occurring plant comprising an ectopically expressed nucleic acid molecule encoding a tomato Bax inhibitor-1 (BI-1) polypeptide or any active fragment thereof, including a tomato BI-1 having substantially the amino acid sequence of SEQ ID NO:4, said plant being characterized by increased resistance to biotic or abiotic stress. The claims are also drawn to a method of increasing the resistance of a plant to biotic or abiotic stress by ectopically expressing in a plant a nucleic acid molecule encoding a tomato BI-1 polypeptide or an active fragment thereof.

Flinn et al. Teach making transgenic plants that express a Bax inhibitor-1 (BI-1) polypeptide of SEQ ID NOS: 87 and 88 (column 1 line 58 through column 2 line 5; column 4 lines 1-9; column 7 lines 53-67; column 9 line 65 column 10 line 24; column 19 line 40 through column 24 line 64). While Flinn et al. do not teach a nucleic acid molecule encoding a Bax inhibitor-1 (BI-1) polypeptide obtained from tomato, the limitation “tomato” imposes no structural imitations on the claimed tomato Bax inhibitor-1 (BI-1) polypeptide that would distinguish a “tomato” Bax inhibitor-1 (BI-1) polypeptide from the Bax inhibitor-1 (BI-1) polypeptides of SEQ ID NOS: 87 and 88. Furthermore, while Flinn et al. do not explicitly teach that transgenic plants expressing a Bax inhibitor-1 (BI-1) polypeptide of SEQ ID NOS: 87 and 88 would be characterized by increased resistance to biotic or abiotic stress, the transgenic plants

expressing a Bax inhibitor-1 (BI-1) polypeptide of SEQ ID NOS: 87 and 88 taught by Flinn et al. would inherently exhibit increased resistance to biotic or abiotic stress, as the rejected claims require only that the plants express a "tomato" Bax inhibitor-1 (BI-1) polypeptide.

Remarks

No claim is allowed.

Claim 31 is deemed free of the prior art due to the failure of the prior art to teach or suggest a plant that ectopically expresses an isolated nucleic acid molecule encoding a polypeptide of SEQ ID NO:4.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



CC
September 25, 2003

AMY J. NELSON, PH.D
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